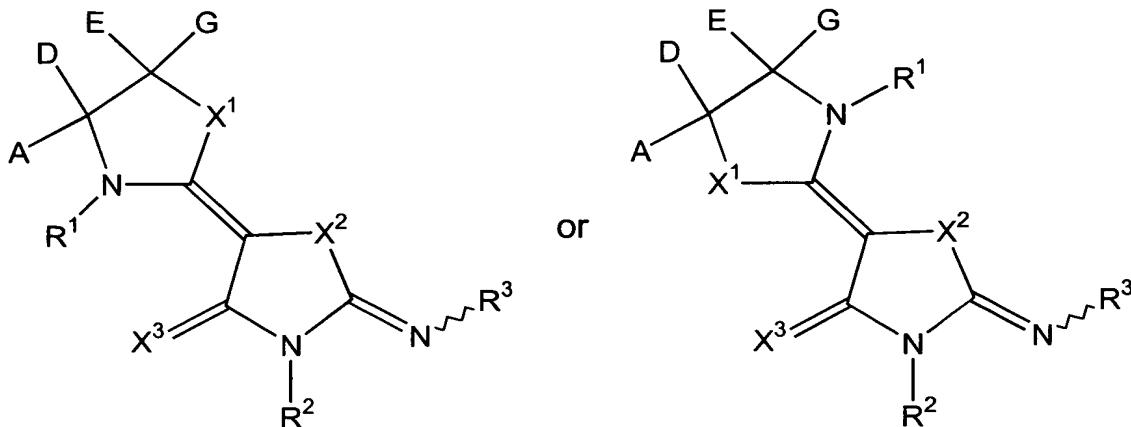


**WHAT IS CLAIMED IS:**

1. A pharmaceutical composition, comprising:  
 (a) a compound of formulae I:



5 or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

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cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl,

5        substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

      (ii)    A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene;

10      and the others of A, D, E and G are selected as in (i);

      X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

      X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

      R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted

15      or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

      R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

25      unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

      where

      R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

15 R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

25 where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or

5 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and

each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;

10 each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,

15 aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,

20 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyoxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

25 dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,

5 alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,

10 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,

15 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

20 each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;  $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form

25 alkylene, azaalkylene, oxaalkylene or thiaalkylene;  $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

30  $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ ; and

(b) one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an anti-hypercholesterolemic agent, a cholesterol

biosynthesis inhibitor, an acyl-coenzyme A:cholesterol acytransferase (ACAT) inhibitor, probucol, raloxifene, nicotinic acid, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant, a low density lipoprotein receptor inducer, clofibrate, fenofibrate, benzofibrate, cipofibrate, gemfibrozil, vitamin

5 B<sub>6</sub>, vitamin B<sub>12</sub>, an anti-oxidant vitamin, a β-blocker, an anti-diabetes agent, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, a fibrinogen receptor antagonist, aspirin or a fibrin acid derivative.

2. The composition of claim 1, wherein the cholesterol biosynthesis 10 inhibitor is an HMG CoA reductase inhibitor.

3. The composition of claim 2, wherein the HMG CoA reductase inhibitor is lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or rivastatin.

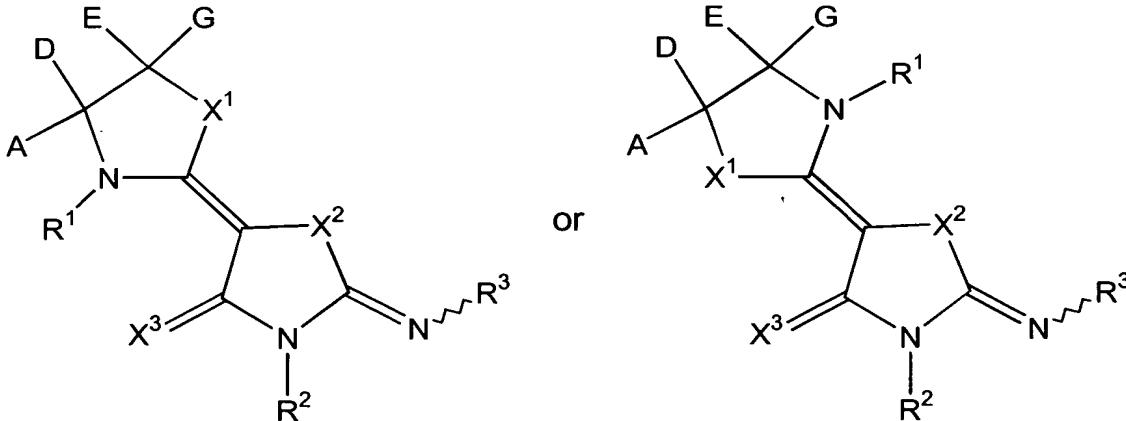
4. The composition of claim 3, wherein the HMG CoA reductase 15 inhibitor is lovastatin or simvastatin.

5. The composition of claim 1, wherein the bile acid sequestrant is an anion exchange resin or a quaternary amine.

6. The composition of claim 1, wherein the quaternary amine is cholestyramine or colestipol.

20 7. A pharmaceutical composition, comprising:

(a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

25 (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 5 substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,  
 10 substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 15 2-aza-1,3-butadienylene;  
 D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
 20 unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or  
 25 (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);  
 X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>,  
 30 Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;  
 X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;  
 R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

5 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

$R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

10 unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted 15 heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;  
where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl,

20 substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

25  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted

30 aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or

5 unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

10 where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or

15 more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl,

20 heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,

25 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy,

30 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N'-arylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-

arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino,

5 alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino,

10 arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

15 hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

20 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or

25 alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and

each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,

30 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl,

aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,

5    arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyoxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy,

10   aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

15   diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'- diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'- triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

20   alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

25   heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,

30   hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,

alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which

5 substitute the same atom, together form alkylene;  
 each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;  
 R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl,

10 aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;  
 R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;  
 R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl,

15 heterocyclyl or heterocyclylalkyl; and  
 R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, and  
 (b) one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an antihypercholesterolemic agent, an HMG-CoA

20 synthase inhibitor, a squalene epoxidase inhibitor, a squalene synthetase inhibitor, an acyl-coenzyme A cholesterol acyltransferase inhibitor, probucol, nicotinic acid or a salt thereof, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant anion exchange resin, a low density lipoprotein receptor inducer, a fibrate, vitamin B<sub>6</sub> or a pharmaceutically acceptable salt

25 thereof, vitamin B<sub>12</sub>, vitamin B<sub>3</sub>, an anti-oxidant vitamin, a beta-blocker, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, or aspirin.

8. The composition of claim 7, wherein the antihypercholesterolemic agent is a cholesterol biosynthesis inhibitor.

30 9. The composition of claim 8, wherein the cholesterol biosynthesis inhibitor is an hydroxymethylglutaryl CoA reductase inhibitor.

10. The composition of claim 9, wherein the hydroxymethylglutaryl CoA reductase inhibitor is lovastatin, simvastatin, pravastatin, fluvastatin, or atorvastatin.

11. The composition of claim 7, wherein the acyl-coenzyme A 5 cholesterol acyltransferase inhibitor is melinamide.

12. The composition of claim 7, wherein the cholesterol absorption inhibitor is  $\beta$ -sitosterol.

13. The composition of claim 7, wherein the bile acid sequestrant anion exchange resin is cholestyramine, colestipol or a dialkylaminoalkyl 10 derivative of a cross-linked dextran.

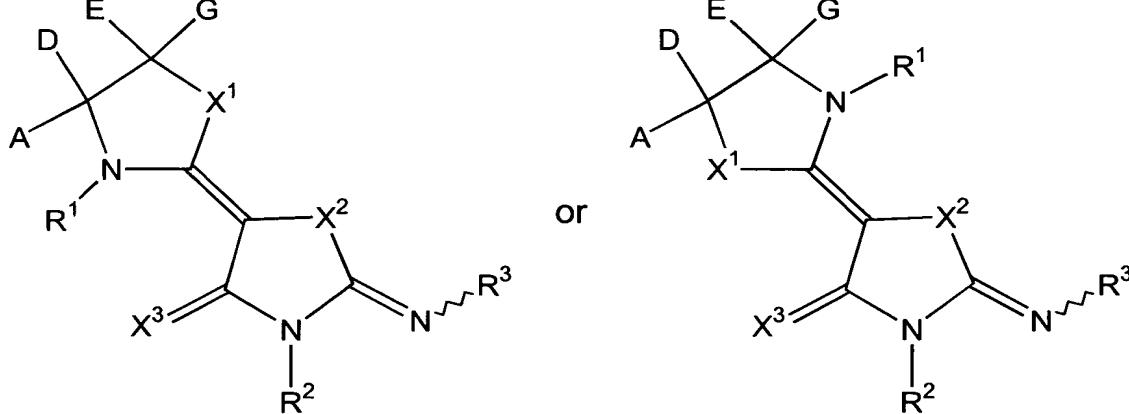
14. The composition of claim 7, wherein the fibrate is clofibrate, bezafibrate, fenofibrate, or gemfibrozil.

15. The composition of claim 7, wherein the anti-oxidant vitamin is vitamin C, vitamin E or beta carotene.

16. The composition of claim 7, wherein the platelet aggregation inhibitor is a fibrinogen receptor antagonist.

17. The composition of claim 16, wherein the fibrinogen receptor antagonist is a glycoprotein IIb/IIIa fibrinogen receptor antagonist.

18. A pharmaceutical composition, comprising:  
20 (a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, 25 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl,

5        substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted

10      oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

15      D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

20      (ii)     A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

25      X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

30      X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

          R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or

unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted

5 heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

$R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted

10 or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

15 where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted

20 cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

25  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

30  $J$  is  $O$ ,  $S$  or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,

substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl,

10 cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,

15 hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene,

20 alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,

25 heterocyclxyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,

30 ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido,

N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, **5** arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminooalkyl, aryloxycarbonylaminooalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, **10** heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, **15** alkylsulfinyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, **20** dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and **25** each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ; each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 **30** double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,

heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl,  
 aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,  
 arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,  
 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,  
**5** aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy,  
 perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy,  
 arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,  
 aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,  
 dialkylaminocarbonyloxy, alkylarylaminoxy, diarylaminocarbonyloxy,  
**10** guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,  
 N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  
 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-  
 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-  
 diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-  
**15** triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,  
 alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,  
 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,  
 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,  
 diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino,  
**20** aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,  
 aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,  
 alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,  
 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  
 $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,  
**25** alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio,  
 perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,  
 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,  
 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy,  
 alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,  
**30** diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl,  
 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,  
 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,  
 diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which

substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more

5 substituents each independently selected from alkyl, halo and pseudohalo;

R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

10 R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>;

15 and

(b) one or more of the following: a sulfonylurea, a biguanides, a thiazolidinedione, an insulin sensitizer, dehydroepiandrosterone or its conjugated sulfate ester, an antiglucocorticoid, a TNF $\alpha$  inhibitor, an  $\alpha$ -glucosidase inhibitor, pramlintide, an insulin secretagogue, or insulin.

20 19. The composition of claim 18, wherein the sulfonylurea is chlorpropamide, tolbutamide, acetohexamide, tolazamide, glyburide, gliclazide, glynase, glimepiride, or glipizide.

20. The composition of claim 18, wherein the biguanide is metformin.

25 21. The composition of claim 18, wherein the thiazolidinedione is ciglitazone, pioglitazone, troglitazone, or rosiglitazone.

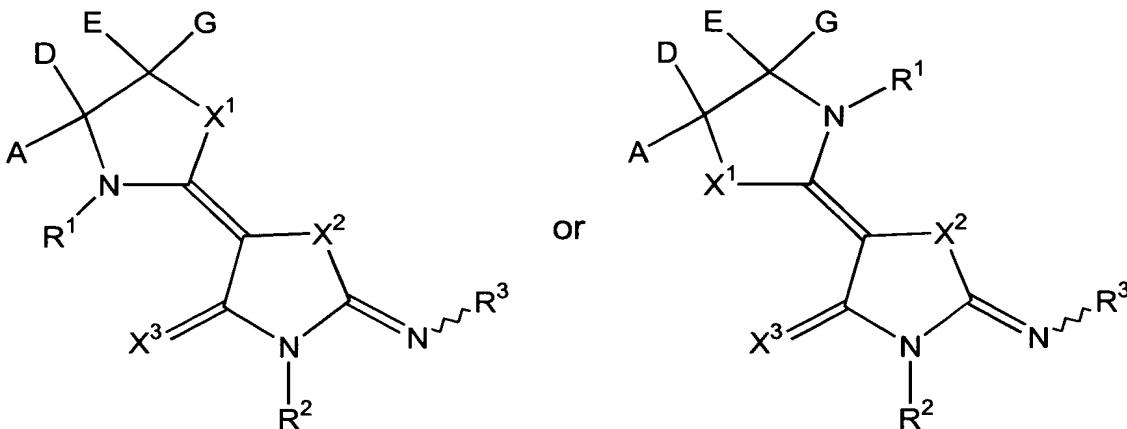
22. The composition of claim 18, wherein the insulin sensitizer is a selective or non-selective activator of PPAR $\alpha$ , PPAR $\beta$  or PPAR $\gamma$ .

23. The composition of claim 18, wherein the  $\alpha$ -glucosidase inhibitor 30 is acarbose, miglitol, or voglibose.

24. The composition of claim 18, wherein the insulin secretagogue is repaglinide, gliquidone, or nateglinide.

25. A pharmaceutical composition, comprising:

(a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

5 (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);  
 $X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>,

10 Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;  
 $X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;  
 $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or

15 unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>,

20 S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;  
 $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl,

25 substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, where

30 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted

cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

5 R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

10 J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,

15 substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

20 R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl,

25 heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl,

30 aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene,

alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,

5 arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynylloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy,

10 alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido,

15 N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, dialkylamino,

20 haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,

25 -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,

30 alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,

dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and

5    each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;

      each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,

10   haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,

15   heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy,

20   perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,

25   N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,

30   alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylarnino, alkylcarbonylarnino, alkoxycarbonylarnino,

aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,

5  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfinyloxy, alkoxy sulfonyloxy, aminosulfinyloxy,

10 alkylaminosulfinyloxy, dialkylaminosulfinyloxy, arylaminosulfinyloxy, diarylaminosulfinyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which

15 substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

20  $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl,

25 heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ ; and

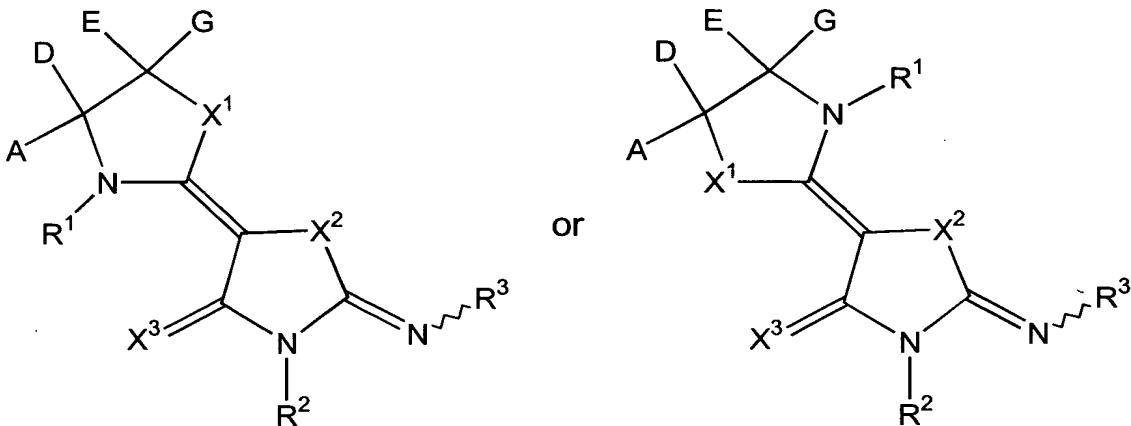
30 (b) one or more of the following: phenylpropanolamine, phentermine, diethylpropion, mazindol, fenfluramine, dexfenfluramine, phentiramine, a  $\beta_3$  adrenoceptor agonist, sibutramine, a gastrointestinal lipase inhibitor, a leptin, neuropeptide Y, enterostatin, cholecytokinin, bombesin,

amylin, a histamine H<sub>3</sub> receptor, a dopamine D<sub>2</sub> receptor, melanocyte stimulating hormone, corticotrophin releasing factor, galanin or gamma amino butyric acid.

26. The composition of claim 25, wherein the gastrointestinal lipase inhibitor is orlistat.

27. A pharmaceutical composition, comprising:

(a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

10 A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or

15

20

25

unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>; where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen,

- 5 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or

- 15 unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

- 20 R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;
- 25

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- 30 where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or

more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl

5 containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl,

10 aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,

15 alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-

20 arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,

25 arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diaryl amino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl, aryloxy carbonyl aminoalkyl, aryloxyaryl carbonylamino,

30 aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,  
 hydroxycarbonylalkylthio, thiocyano, isothiocyanato, alkylsulfinyloxy,  
 alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,  
 alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,

5 dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
 hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,  
 dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
 alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or

10 1,3 arrangement, together form alkylene dioxy, thioalkylene oxy or  
 alkylene dithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the  
 same atom, together form alkylene; and  
 each Q<sup>1</sup> is independently unsubstituted or substituted with one or more  
 substituents each independently selected from Q<sup>2</sup>;

15 each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,  
 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,  
 haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2  
 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,  
 cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,

20 aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,  
 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,  
 heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl,  
 aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,  
 arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,

25 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,  
 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxyloxy, cycloalkoxy,  
 perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy,  
 arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy,  
 aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

30 dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy,  
 guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,  
 N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  
 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,

5 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,

10 alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,

15 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfinyloxy, alkoxy sulfonyloxy, aminosulfinyloxy, alkylaminosulfinyloxy, dialkylaminosulfinyloxy, arylaminosulfinyloxy, diarylaminosulfinyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,

20 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

25 each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo; R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or R<sup>70</sup> and R<sup>71</sup> together form

30 alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

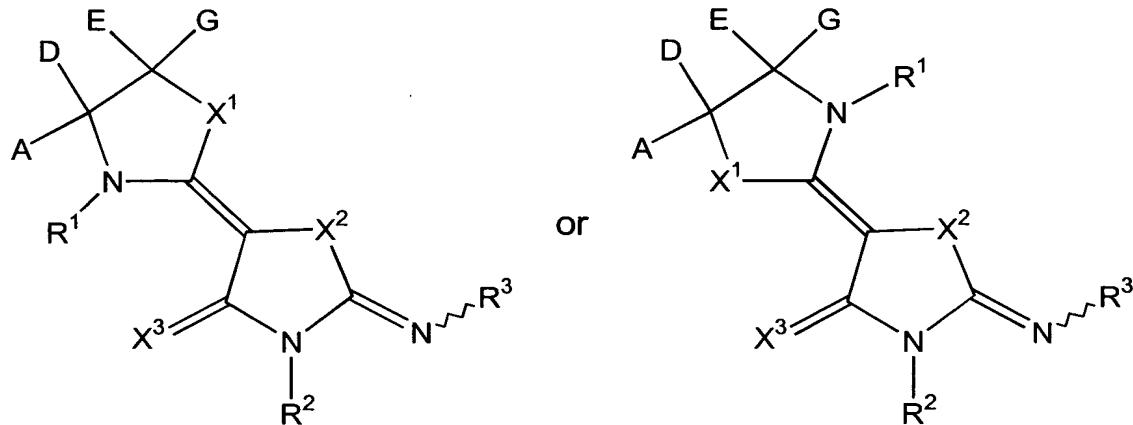
$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and

5 (b) one or more of the following: ursodeoxycholic acid, a corticosteroid, an anti-infective agent, an anti-viral agent, vitamin D, vitamin A, phenobarbital, cholestyramine, UV light, ab antihistamine, an oral opiate receptor antagonist or a biphosphate.

28. The composition of claim 27, wherein the anti-infective agent is  
10 rifampin, rifadin, or rimactane.

29. A method for decreasing hyperglycemia and/or insulin resistance, comprising administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

15 A, D, E and G are selected from (i) or (ii) as follows:  
 (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,  
 20 or A and G together form substituted or unsubstituted alkylene,  
 25 or A and G together form substituted or unsubstituted alkylene,

substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

20  $X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;  
 $X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

25  $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

30  $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

5 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

10 substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo,  
15 pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ,

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

20 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl,

25 substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or  
30 unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ,

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or

5 more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,

10 heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,

15 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy,

20 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-

25 dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

30 arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diaryl amino, alkylaryl amino, alkylcarbonyl amino, alkoxy carbonyl amino, aralkoxy carbonyl amino, aryl carbonyl amino, aryl carbonyl aminoalkyl, aryloxy carbonyl aminoalkyl, aryloxyaryl carbonyl amino,

aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

5 hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxyssulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

10 alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxyssulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or

15 alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and

each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,

20 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,

25 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,

30 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

5 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

10 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

15 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,

20 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,

25 diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more

30 substituents each independently selected from alkyl, halo and pseudohalo; R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl,

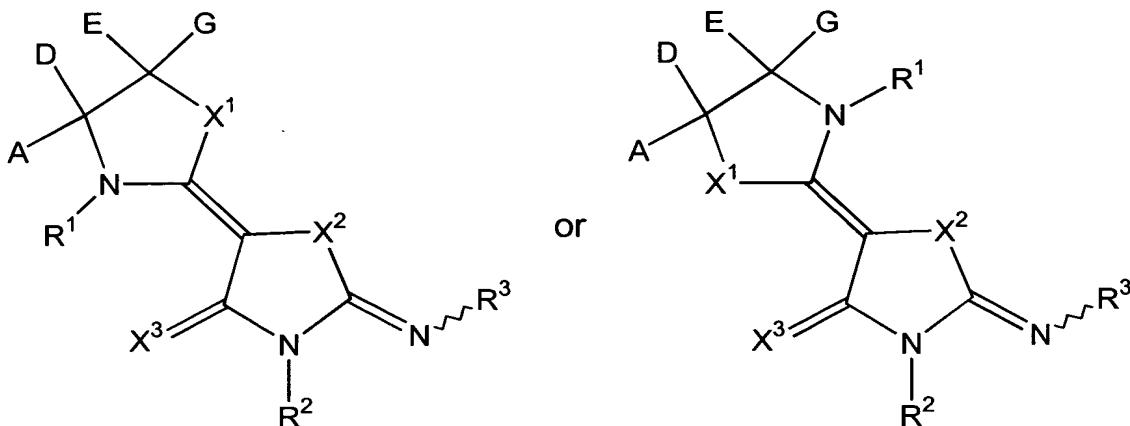
aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

5  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

30. A method for treatment, prevention or amelioration of one or more symptoms or complications of type II diabetes, comprising administering  
10 a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen,

15 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or

20 unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,

25 substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

5           D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

10           (ii)    A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

15           X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

20           X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

          R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

25           substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

30           R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

5 where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted

10 cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or

15 unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is  $O$ ,  $S$  or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted

25 heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl,

30 alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl,

heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,

5 hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene,

10 alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,

15 heterocyclxyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminoxyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,

20 ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,

25 arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamin, alkylarylamino, alkylcarbonylamino,

30 alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminooalkyl, aryloxycarbonylaminooalkyl, aryloxyarylcarbonylaminoo, aryloxycarbonylaminoo, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,

$\text{-N}^+\text{R}^{51}\text{R}^{52}\text{R}^{53}$ ,  $\text{P}(\text{R}^{50})_2$ ,  $\text{P}(\text{=O})(\text{R}^{50})_2$ ,  $\text{OP}(\text{=O})(\text{R}^{50})_2$ ,  $\text{-NR}^{60}\text{C}(\text{=O})\text{R}^{63}$ ,  
 dialkylphosphonyl, alkylarylphtosphonyl, diarylphosphonyl,  
 hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,  
 hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy,  
**5** alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,  
 alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,  
 dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
 hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,  
**10** dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
 alkylarylamino sulfonyl; or two  $\text{Q}^1$  groups, which substitute atoms in a 1,2 or  
 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or  
 alkylenedithioxy where  $\text{y}$  is 1 or 2; or two  $\text{Q}^1$  groups, which substitute the  
 same atom, together form alkylene; and  
**15** each  $\text{Q}^1$  is independently unsubstituted or substituted with one or more  
 substituents each independently selected from  $\text{Q}^2$ ;  
     each  $\text{Q}^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,  
 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,  
 haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2  
**20** double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,  
 cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,  
 aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,  
 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,  
 heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl,  
**25** aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,  
 arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,  
 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,  
 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxyloxy, cycloalkoxy,  
 perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy,  
**30** arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy,  
 aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,  
 dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy,  
 guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,

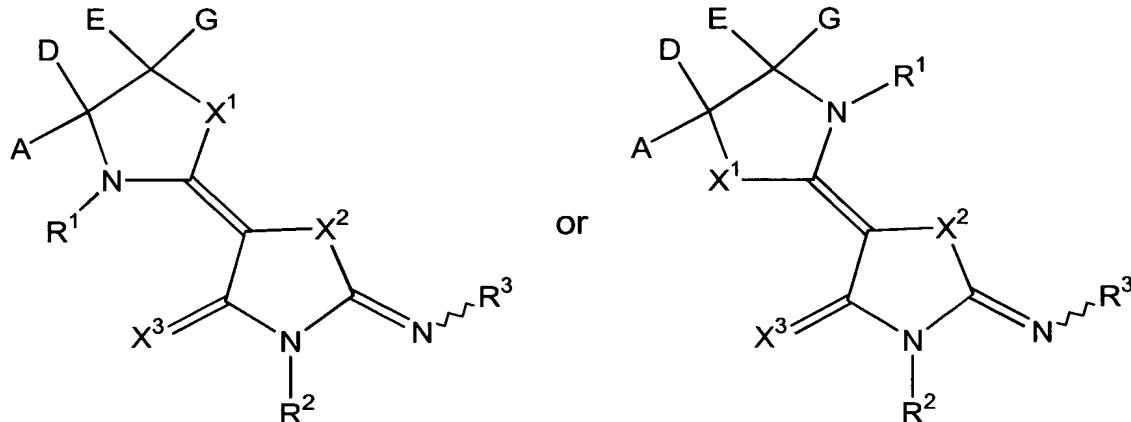
N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  
 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-  
 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-  
 diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-  
 5 triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,  
 alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,  
 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,  
 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,  
 diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino,  
 10 aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,  
 aryloxy carbonylaminoalkyl, aryloxy aryl carbonylamino, aryloxy carbonylamino,  
 alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino,  
 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  
 $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,  
 15 alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio,  
 perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,  
 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,  
 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy,  
 alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,  
 20 diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl,  
 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,  
 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,  
 diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which  
 substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy,  
 25 thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which  
 substitute the same atom, together form alkylene;  
 each  $Q^2$  is independently unsubstituted or substituted with one or more  
 substituents each independently selected from alkyl, halo and pseudohalo;  
 $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  
 30  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl,  
 aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form  
 alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

5  $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ .

31. A method of modulating atherosclerosis, comprising administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

10 A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_{2}R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or

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20

25

unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

$R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>; where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen,

- 5 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or

- 15 unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

- 20 R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- 30 where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or

more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl

5 containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl,

10 aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,

15 alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-

20 arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,

25 arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diaryl aminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diaryl amino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl, aryloxy carbonyl aminoalkyl, aryloxyarylcarbonylamino,

30 aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,  
 hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfinyloxy,  
 alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,  
 alkoxyssulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,

5 dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
 alkylarylaminoosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
 hydroxysulfonyl, alkoxyssulfonyl, aminosulfonyl, alkylaminosulfonyl,  
 dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
 alkylarylaminoosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or

10 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or  
 alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the  
 same atom, together form alkylene; and  
 each Q<sup>1</sup> is independently unsubstituted or substituted with one or more  
 substituents each independently selected from Q<sup>2</sup>;

15 each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,  
 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,  
 haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2  
 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,  
 cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,

20 aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,  
 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,  
 heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl,  
 aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,  
 arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,

25 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,  
 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy,  
 perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy,  
 arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy,  
 aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

30 dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy,  
 guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,  
 N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  
 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,

5 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,

10 alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocano, isothiocano,

15 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,

20 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

25 each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo; R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or R<sup>70</sup> and R<sup>71</sup> together form

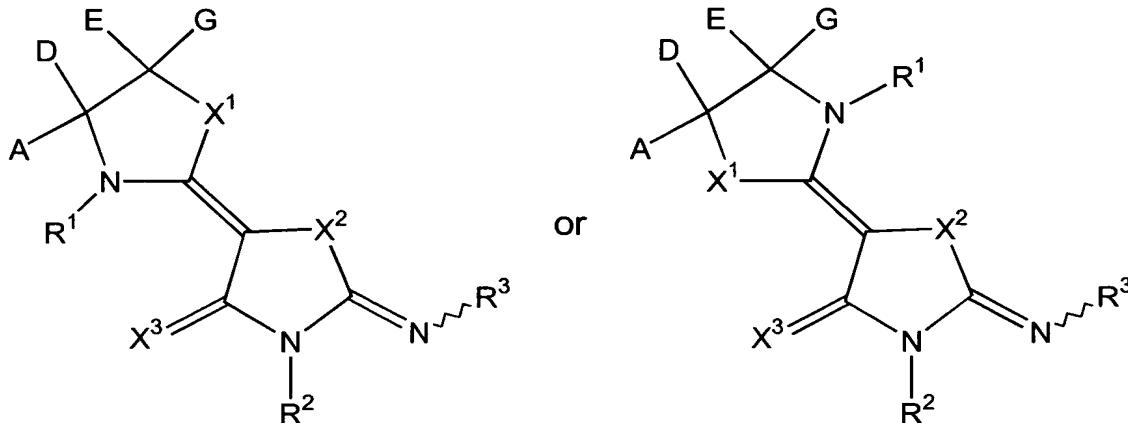
30 alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

32. A method of treating, preventing, or ameliorating obesity or  
5 complications thereof, comprising administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen,

10 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,

15 substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

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25

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);  
 $X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>,

**15** Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;  
 $X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;  
 $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>,

**20** **25** S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;  
 $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl,

**30** substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted

heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;  
where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

- 5 substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo,
- 10 pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

- 15 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ,

$J$  is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl,

- 20 substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;
- 25

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl,

- 30 cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo,

pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,

5 heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,

10 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy,

15 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-

20 dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

25 arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl, aryloxy carbonyl aminoalkyl, aryloxyaryl carbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino,

30 heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,

hydroxycarbonylalkylthio, thiocyano, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

5 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylene dioxy, thioalkylene oxy or

10 alkylene dithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and

each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;

each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,

15 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl,

20 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,

25 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy,

30 guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-

diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

5 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

10 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,

15 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,

20 diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

each  $Q^2$  is independently unsubstituted or substituted with one or more

25 substituents each independently selected from alkyl, halo and pseudohalo;  $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

30  $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

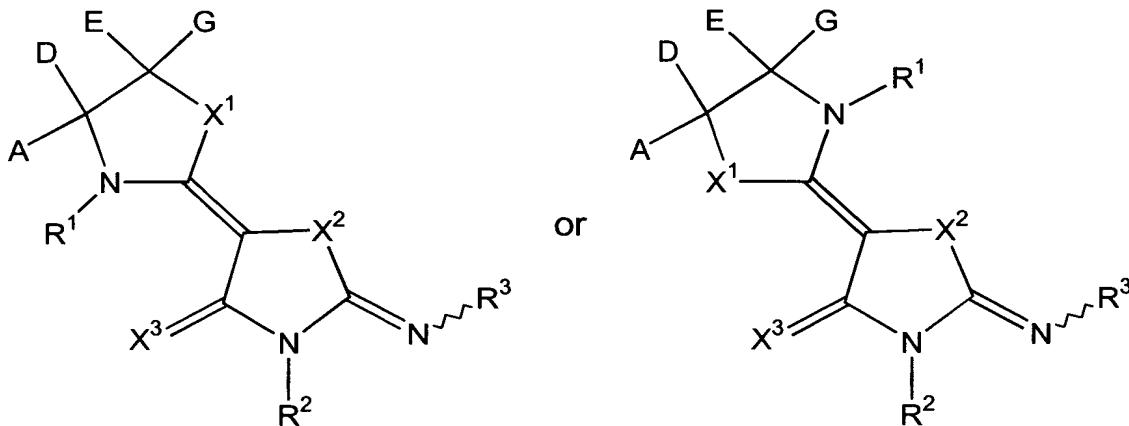
$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

33. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated,

5 comprising administering a pharmaceutical composition of claim 1.

34. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated, comprising:

10 (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,

15 20 25 substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

5           D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

10           (ii)    A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

15           X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

20           X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

            R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

25           substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

30           R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

5 where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted

10 cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or

15 unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

20 aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted

25 heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl,

30 alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl,

heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,

5 hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene,

10 alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,

15 heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,

20 ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,

25 arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino,

30 alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl, aryloxy carbonyl aminoalkyl, aryloxyaryl carbonyl amino, aryloxy carbonyl amino, alkylsulfonyl amino, arylsulfonyl amino, heteroaryl sulfonyl amino, heterocyclsulfonyl amino, heteroarylthio, azido,

$\text{-N}^+\text{R}^{51}\text{R}^{52}\text{R}^{53}$ ,  $\text{P}(\text{R}^{50})_2$ ,  $\text{P}(=\text{O})(\text{R}^{50})_2$ ,  $\text{OP}(=\text{O})(\text{R}^{50})_2$ ,  $\text{-NR}^{60}\text{C}(=\text{O})\text{R}^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyanato, alkylsulfinyloxy,

**5** alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,

**10** dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $\text{Q}^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkyleneoxy or alkylenedithioxy where  $\text{y}$  is 1 or 2; or two  $\text{Q}^1$  groups, which substitute the same atom, together form alkylene; and

**15** each  $\text{Q}^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $\text{Q}^2$ ;  
 each  $\text{Q}^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2

**20** double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl,

**25** aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy,

**30** arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,

N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  
 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-  
 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-  
 diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-  
 5 triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,  
 alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,  
 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,  
 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,  
 diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino,  
 10 aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,  
 aryloxy carbonylaminoalkyl, aryloxy aryl carbonylamino, aryloxy carbonylamino,  
 alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino,  
 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  
 $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,  
 15 alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio,  
 perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,  
 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,  
 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy,  
 alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,  
 20 diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl,  
 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,  
 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,  
 diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which  
 substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy,  
 25 thioalkyleneoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which  
 substitute the same atom, together form alkylene;  
 each  $Q^2$  is independently unsubstituted or substituted with one or more  
 substituents each independently selected from alkyl, halo and pseudohalo;  
 $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  
 30  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl,  
 aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form  
 alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

5  $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ ; and

(b) simultaneously, subsequently, or previously administering one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an anti-hypercholesterolemic agent, a cholesterol biosynthesis

10 inhibitor, an acyl-coenzyme A:cholesterol acytransferase (ACAT) inhibitor, probucol, raloxifene, nicotinic acid, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant, a low density lipoprotein receptor inducer, clofibrate, fenofibrate, benzofibrate, cipofibrate, gemfibrozil, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, an anti-oxidant vitamin, a  $\beta$ -blocker, an anti-diabetes agent, an  
 15 angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, a fibrinogen receptor antagonist, aspirin or a fibrin acid derivative.

35. The method of claim 33, wherein the disease or disorder is selected from hypercholesterolemia, hyperlipoproteinemia,

20 hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia,  
 25 cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

36. The method of claim 34, wherein the disease or disorder is selected from hypercholesterolemia, hyperlipoproteinemia,

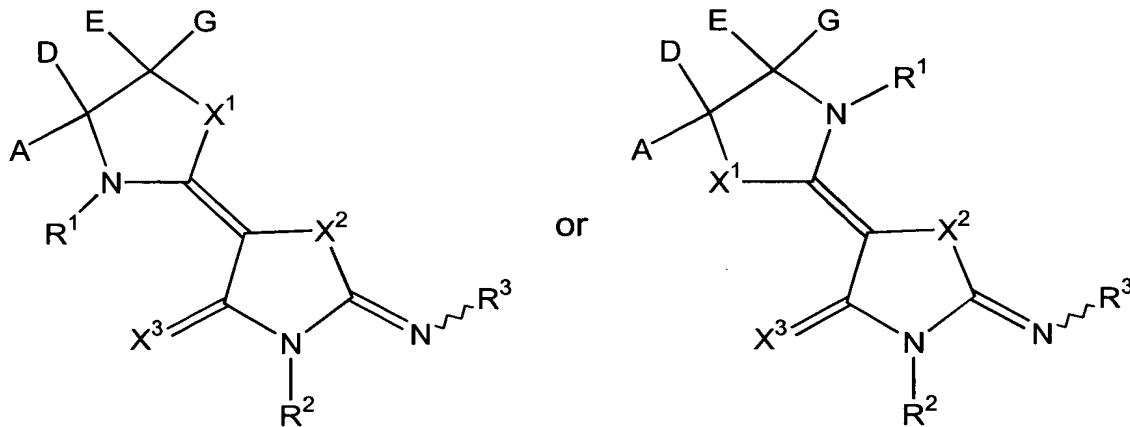
30 hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions

characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

5 37. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder which is affected by cholesterol, triglyceride, or bile acid levels, comprising administering a pharmaceutical composition of claim 1.

38. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder which is affected by cholesterol, triglyceride, or bile acid levels, comprising:

(a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

15 A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,

20

25

substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

5 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ; where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

10 substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo,

15 pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

20 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is  $O$ ,  $S$  or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl,

25 substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or

30 unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or

5 more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,

10 heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,

15 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy,

20 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-

25 dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

30 arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diaryl amino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl, aryloxy carbonyl aminoalkyl, aryloxyaryl carbonyl amino,

aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

5 hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxyssulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

10 alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxyssulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or

15 alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and

each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,

20 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heterarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,

25 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,

30 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

5 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

10 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

15 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,

20 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,

25 diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more

30 substituents each independently selected from alkyl, halo and pseudohalo; R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl,

aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

5  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

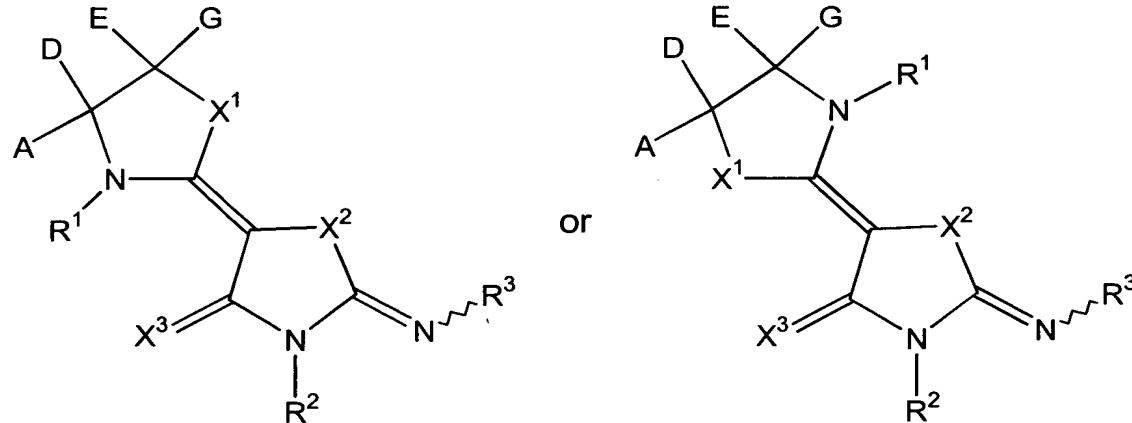
$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and

10 (b) simultaneously, subsequently, or previously administering one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an anti-hypercholesterolemic agent, a cholesterol biosynthesis inhibitor, an acyl-coenzyme A:cholesterol acytransferase (ACAT) inhibitor, probucol, raloxifene, nicotinic acid, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant, a low density lipoprotein receptor inducer, 15 clofibrate, fenofibrate, benzofibrate, cipofibrate, gemfibrozil, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, an anti-oxidant vitamin, a  $\beta$ -blocker, an anti-diabetes agent, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, a fibrinogen receptor antagonist, aspirin or a fibrin acid derivative.

20 39. A method for decreasing hyperglycemia and/or insulin resistance, comprising administering the pharmaceutical composition of claim 18.

40 A method for decreasing hyperglycemia and/or insulin resistance, comprising:

25 (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;
- (ii) D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted

- 5 or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;
- 10  $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;
- 15 where
- 20

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl,

- 25 substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

- 30  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is O, S or  $NR^{14}$ ;

5         $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

10      where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo,

15      20      pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl,

25      30      trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy,

aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy,  
 alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,  
 ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-  
 N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-  
 5 arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-  
 dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido,  
 N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,  
 arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino,  
 alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,  
 10 arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,  
 arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino,  
 haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino,  
 alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino,  
 arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino,  
 15 aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino,  
 heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  
 -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>,  
 dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,  
 hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,  
 20 hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy,  
 alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,  
 alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,  
 dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
 25 hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,  
 dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
 alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or  
 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or  
 alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the  
 30 same atom, together form alkylene; and  
 each Q<sup>1</sup> is independently unsubstituted or substituted with one or more  
 substituents each independently selected from Q<sup>2</sup>;

each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,

5     cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,

10    arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,

15    aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

20    diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

25    alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminooalkyl, aryloxycarbonylaminooalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

30    heterocyclsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,

alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl,

5 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which

10 substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl,

15 aryl, heteroaryl, heteroaralkyl or heterocycl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl,

20 heterocycl or heterocyclalkyl; and

R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or -NR<sup>70</sup>R<sup>71</sup>; and

(b) subsequently, simultaneously, or previously administering one or more of the following: a sulfonylurea, a biguanides, a thiazolidinedione, an

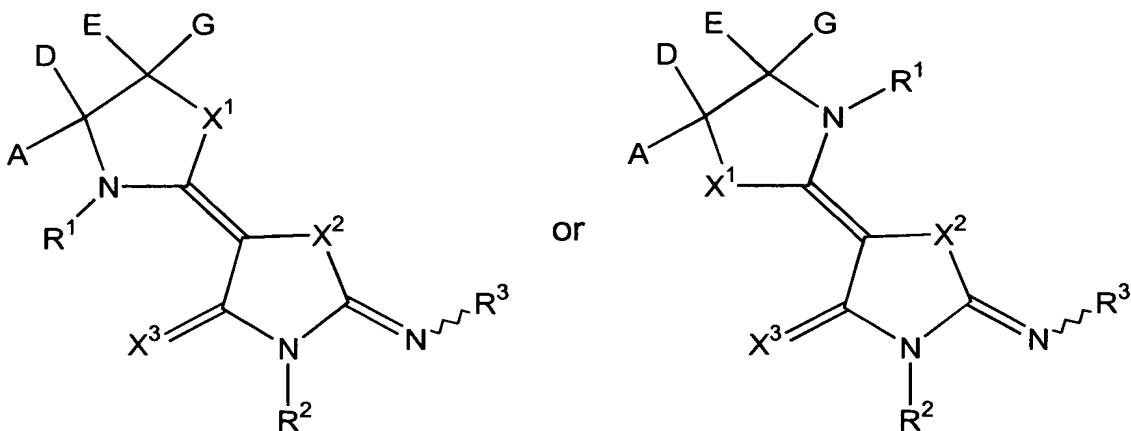
25 insulin sensitizer, dehydroepiandrosterone or its conjugated sulfate ester, an antiglucocorticoid, a TNF $\alpha$  inhibitor, an  $\alpha$ -glucosidase inhibitor, pramlintide, an insulin secretagogue, or insulin.

41. A method for treatment, prevention or amelioration of one or more symptoms or complications of type II diabetes, comprising administering

30 a pharmaceutical composition of claim 18.

42. A method for treatment, prevention or amelioration of one or more symptoms or complications of type II diabetes, comprising:

(a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen,

5 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or

10 unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene

15 substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene:

25 D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

5  $X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

10  $X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

15 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

20 R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl,

25 substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen,

30 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or

unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or

- 5 unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;
- 10 J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted

- 15 heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl,

- 20 alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>,

- 25 R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl

- 30 containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl,

alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,

**5** heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino, carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,

**10** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,

**15** arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamin, alkylarylamino, alkylcarbonylamino,

**20** alkoxy, carbonylamin, aralkoxy, carbonylamin, arylcarbonylamin, arylcarbonylamin, alkylcarbonylamin, aryloxycarbonylamin, alkylsulfonylamin, arylsulfonylamin, heteroarylsulfonylamin, heterocyclsulfonylamin, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ ,

**25** dialkylphosphonyl, alkylarylphtosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyan, isothiocyan, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,

**30** dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or

alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and

- 5        each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>:
  - each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2
- 10      double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 20      alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diaryl amino, alkylaryl amino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl,
- 25      N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 30      alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diaryl amino, alkylaryl amino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl,

aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,

5 alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,

10 diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy,

15 thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

$R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or

20  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

25  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ ; and

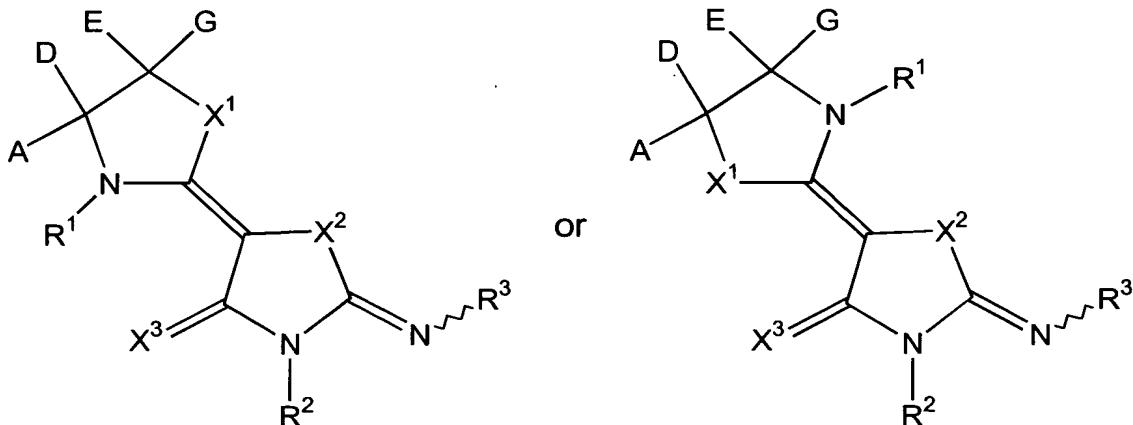
(b) subsequently, simultaneously, or previously administering one

30 or more of the following: a sulfonylurea, a biguanides, a thiazolidinedione, an insulin sensitizer, dehydroepiandrosterone or its conjugated sulfate ester, an antiglucocorticoid, a  $TNF\alpha$  inhibitor, an  $\alpha$ -glucosidase inhibitor, pramlintide, an insulin secretagogue, or insulin.

43. A method of modulating atherosclerosis, comprising administering a pharmaceutical composition of claim 7.

44. A method of modulating atherosclerosis, comprising:

(a) administering a compound of formulae I:



5

or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

10 25 D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

10  $X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

15 R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted

20 aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or

25 unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

30 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted

5 cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or

10 unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

15  $J$  is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted

20 heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl,

25 alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,

30  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl,

aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene,

**5** alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,

**10** heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,

**15** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,

**20** arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino,

**25** alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonyl aminoalkyl, aryloxycarbonyl aminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ ,

**30** dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,

alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,  
 dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
 hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,

5 dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
 alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or  
 1,3 arrangement, together form alkylene dioxy, thioalkylene oxy or  
 alkylene dithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the  
 same atom, together form alkylene; and

10 each Q<sup>1</sup> is independently unsubstituted or substituted with one or more  
 substituents each independently selected from Q<sup>2</sup>;  
 each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,  
 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,  
 haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2

15 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,  
 cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,  
 aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,  
 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,  
 heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl,  

20 aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,  
 arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,  
 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,  
 aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy,  
 perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy,

25 arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxycarbonyloxy,  
 aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,  
 dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy,  
 guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,  
 N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  

30 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-  
 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-  
 diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-  
 triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,

alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino,

5 aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,

10 alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxyssulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,

15 diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxyssulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy,

20 thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

$R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or

25  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocycl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl;

30  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycl or heterocyclalkyl; and

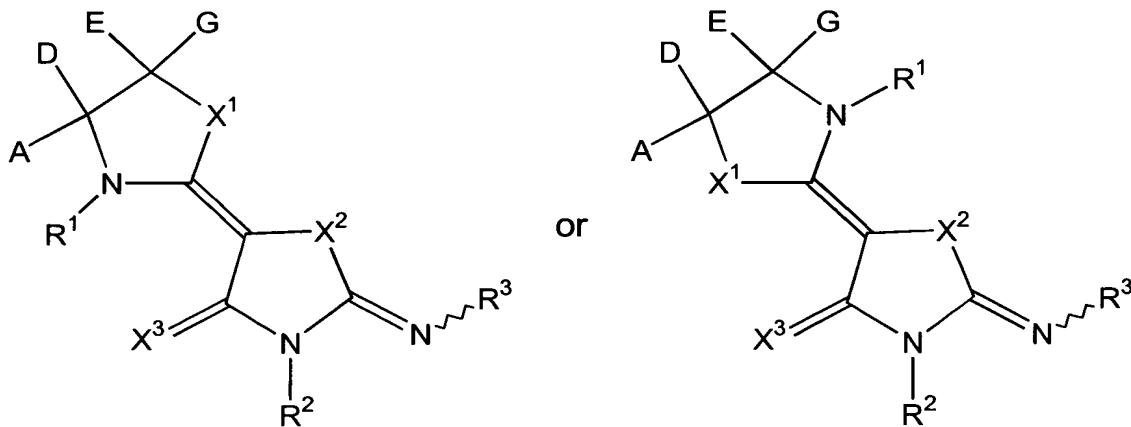
$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocycl, aryl or  $-NR^{70}R^{71}$ , and

(b) subsequently, simultaneously, or previously administering one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an antihypercholesterolemic agent, an HMG-CoA synthase inhibitor, a squalene epoxidase inhibitor, a squalene synthetase inhibitor, an acyl-  
 5 coenzyme A cholesterol acyltransferase inhibitor, probucol, nicotinic acid or a salt thereof, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant anion exchange resin, a low density lipoprotein receptor inducer, a fibrate, vitamin B<sub>6</sub> or a pharmaceutically acceptable salt thereof, vitamin B<sub>12</sub>, vitamin B<sub>3</sub>, an anti-oxidant vitamin, a beta-blocker, an angiotensin II  
 10 antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, or aspirin.

45. A method of treating, preventing, or ameliorating obesity or complications thereof, comprising administering a pharmaceutical composition of claim 25.

15 46. A method of treating, preventing, or ameliorating obesity or complications thereof, comprising:

(a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

20 A, D, E and G are selected from (i) or (ii) as follows:  
 (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or  
 25

unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 substituted or unsubstituted heteroaralkyl, substituted or unsubstituted  
 heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo,  
 pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>,  
 5 or A and G together form substituted or unsubstituted alkylene,  
 substituted or unsubstituted azaalkylene, substituted or unsubstituted  
 oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or  
 unsubstituted alkenylene, substituted or unsubstituted alkynylene,  
 substituted or unsubstituted 1,3-butadienylene, substituted or  
 10 unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted  
 2-aza-1,3-butadienylene;  
 D and E are each independently selected from hydrogen,  
 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
 substituted or unsubstituted alkynyl, substituted or unsubstituted  
 15 cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
 unsubstituted cycloalkylalkyl, substituted or unsubstituted  
 heterocyclylalkyl, substituted or unsubstituted aryl, substituted or  
 unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D  
 20 and E together form a bond; or  
 (ii) A and D; or E and G; together form substituted or unsubstituted  
 alkylene, substituted or unsubstituted azaalkylene, substituted or  
 unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene;  
 and the others of A, D, E and G are selected as in (i);  
 25 X<sup>1</sup> and X<sup>2</sup> are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>,  
 Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;  
 X<sup>3</sup> is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;  
 R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted  
 or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or  
 30 unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or  
 unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,  
 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted  
 aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or

- 5 unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted
- 10 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

- 15 substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo,
- 20 pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

- 25 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl,

- 30 substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or

or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl,

5 heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or

10 more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,

hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,

15 heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,

20 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy,

25 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N,N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-

30 dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,

arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino,

5 arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphtosphonyl, diarylphosphonyl,

10 hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

15 alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or

20 alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and

each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,

25 nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,

30 triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,

arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyoxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,

5 aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

10 diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

15 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

20 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,

25 hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,

30 diarylaminosulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where  $y$  is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

$R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl,

5 aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl,

10 heterocyclyl or heterocyclylalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ;

and

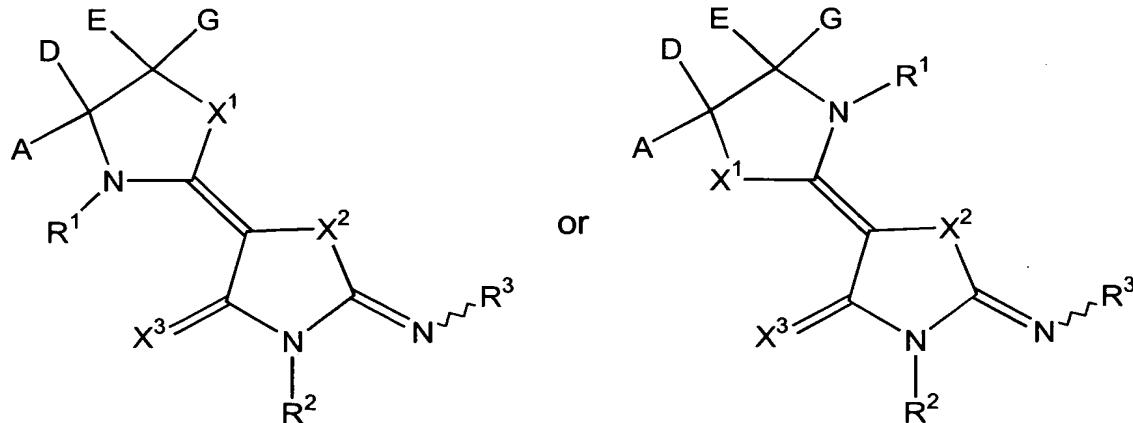
(b) subsequently, simultaneously, or previously administering one or more of the following: phenylpropanolamine, phentermine, diethylpropion,

15 mazindol, fenfluramine, dexfenfluramine, phentiramine, a  $\beta_3$  adrenoceptor agonist, sibutramine, a gastrointestinal lipase inhibitor, a leptin, neuropeptide Y, enterostatin, cholecytokinin, bombesin, amylin, a histamine  $H_3$  receptor, a dopamine  $D_2$  receptor, melanocyte stimulating hormone, corticotrophin releasing factor, galanin or gamma amino butyric acid.

20 47. A method of treating, preventing, or ameliorating one or more symptoms of cholestasis, comprising administering a pharmaceutical composition of claim 27.

48. A method of treating, preventing, or ameliorating one or more symptoms of cholestasis, comprising:

25 (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

5 D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

10 (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

15

20

25

30

$X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted

- 5 or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;
- 10  $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;
- 15 where
- 20

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl,

- 25 substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

- 30  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

$J$  is O, S or  $NR^{14}$ ;

5         $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

15      where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo,

20      pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl,

25      trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,

30      arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy,

aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-ary lureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-ary lureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, 10 arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, 15 aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, 20 hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, 25 hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the 30 same atom, together form alkylene; and each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;

each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,

5    cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,

10    arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,

15    aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminothiocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

20    diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

25    alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminolalkyl, aryloxycarbonylaminolalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

30    heterocyclsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphtosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,

alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl,

5 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which

10 substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl,

15 aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl,

20 heterocyclyl or heterocyclylalkyl; and

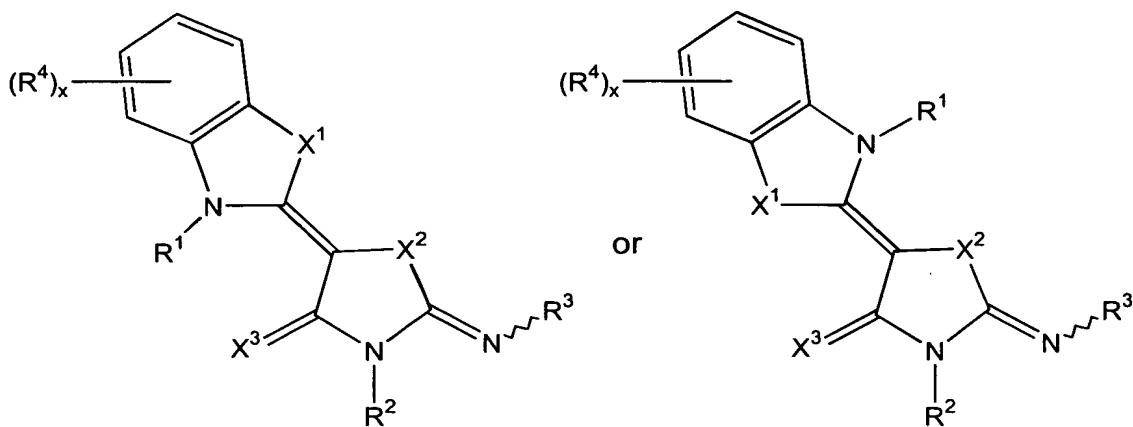
R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>; and

(b) subsequently, simultaneously, or previously administering one or more of the following: ursodeoxycholic acid, a corticosteroid, an anti-

25 infective agent, an anti-viral agent, vitamin D, vitamin A, phenobarbital, cholestyramine, UV light, ab antihistamine, an oral opiate receptor antagonist or a biphosphate.

49. A method of treating, preventing, or ameliorating the symptoms of a disease or disorder that is modulated or otherwise affected by nuclear

30 receptor activity or in which nuclear receptor activity is implicated, comprising administering a compound of formulae III:



or a pharmaceutically acceptable derivative thereof, wherein:

each R<sup>4</sup> is independently substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted guanidino, substituted or unsubstituted isothioureido, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> or C(=J)R<sup>13</sup>;

x is an integer from 0 to 4; and

the amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of R<sup>4</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>.

50. The method of claim 49, wherein X<sup>2</sup> is S and X<sup>3</sup> is O.

20 51. The method of claim 50, wherein X<sup>1</sup> is S.

52. The method of claim 51, wherein R<sup>1</sup> is substituted or unsubstituted alkyl.

53. The method of claim 52, wherein R<sup>2</sup> is substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl.

25 54. The method of claim 53, wherein R<sup>3</sup> is substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

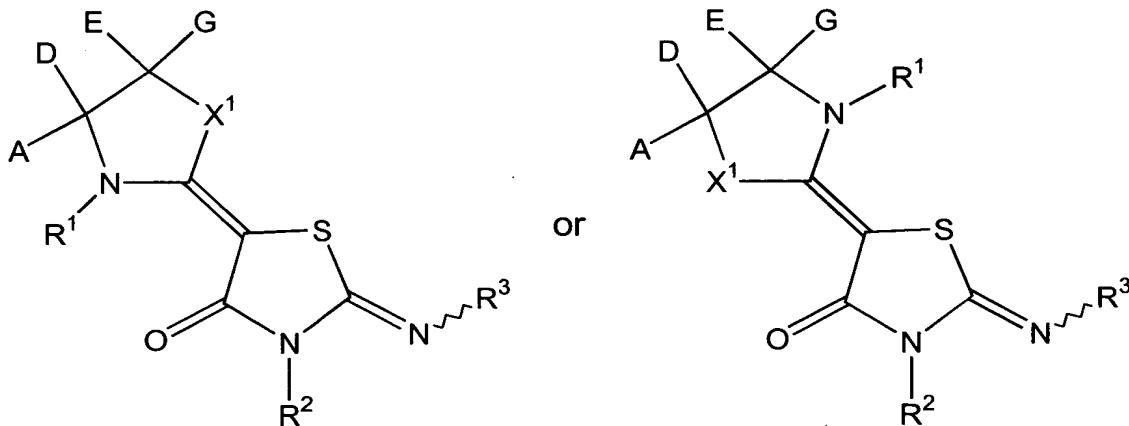
55. The method of claim 50, wherein  $X^1$  is  $CR^8=CR^9$ .

56. The method of claim 55, wherein  $R^1$  is substituted or unsubstituted alkyl.

57. The method of claim 56, wherein  $R^2$  is substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl.

58. The method of claim 57, wherein  $R^3$  is substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

59. A method of treating, preventing, or ameliorating the symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated, comprising administering a compound of formulae II:



or a pharmaceutically acceptable derivative thereof, wherein:

A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_{2}R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond;

- 5       $X^1$  is S;  
 $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,
- 10     substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- 15      $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl,
- 20     substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;  
where:  
 $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen,
- 25     substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;  
 $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or

unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

5 aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted

10 heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl,

15 alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,

20  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl

25 containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl,

30 aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy,

aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,  
 alkoxy carbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy,  
 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy,  
 alkylarylamino carbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,  
**5** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-  
 N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-  
 arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-  
 dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido,  
 N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,  
**10** arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl,  
 arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,  
 arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino,  
 haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino,  
 alkoxy carbonylamino, aralkoxycarbonylamino, arylcarbonylamino,  
**15** arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino,  
 aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino,  
 heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  
 $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ ,  
 dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,  
**20** hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,  
 hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy,  
 alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,  
 alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,  
 dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
**25** alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
 hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,  
 dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
 alkylarylamino sulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or  
 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or  
**30** alkylenedithioxy; or two  $Q^1$  groups, which substitute the same atom, together  
 form alkylene;  
 each  $Q^1$  is independently unsubstituted or substituted with one or more  
 substituents each independently selected from  $Q^2$ ;

each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,

5    cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,

10    arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxyoxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,

15    aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

20    diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

25    alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminooalkyl, aryloxycarbonylaminooalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,

30    heterocyclsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,

alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl,

5 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylene dioxy (i.e., -O-(CH<sub>2</sub>)<sub>y</sub>-O-), thioalkylene oxy (i.e., -S-(CH<sub>2</sub>)<sub>y</sub>-O-) or alkylene dithioxy (i.e., -S-(CH<sub>2</sub>)<sub>y</sub>-S-) where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

10 R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

15 R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

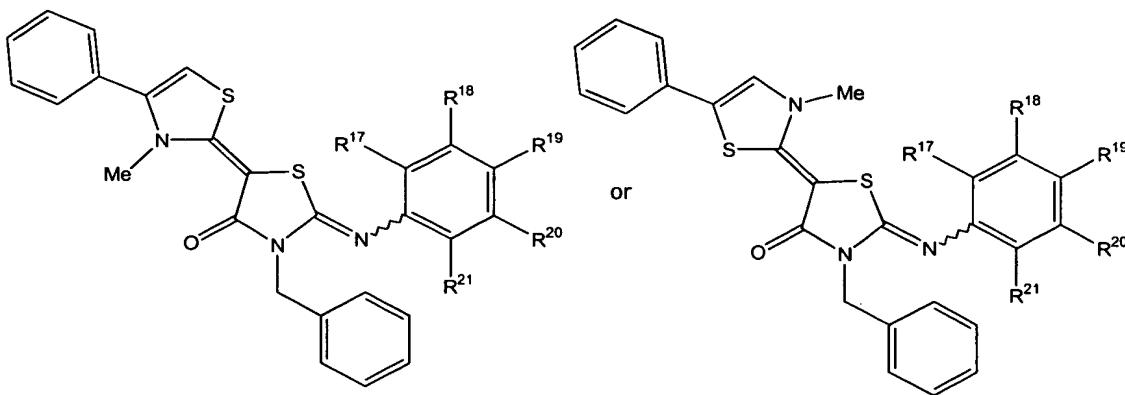
20 R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>.

60. The method of claim 59, wherein R<sup>1</sup> is substituted or unsubstituted alkyl.

61. The method of claim 60, wherein R<sup>2</sup> is substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl.

25 62. The method of claim 61, wherein R<sup>3</sup> is substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

63. The method of claim 59, wherein the compound has formulae VI:



or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl,

- 5 hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl,
- 10 arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,
- 15 heterocyclyoxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 20 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,
- 25 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,

diaryl amino, alkyl aryl amino, alkyl carbonyl amino, alkoxy carbonyl amino, aralkoxy carbonyl amino, aryl carbonyl amino, aryl carbonyl amino alkyl, aryloxycarbonyl amino alkyl, aryloxy aryl carbonyl amino, aryloxycarbonyl amino, alkylsulfonyl amino, arylsulfonyl amino, heteroaryl sulfonyl amino,

5 heterocyclsulfonyl amino, heteroaryl thio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkyl phosphonyl, alkyl aryl phosphonyl, diaryl phosphonyl, hydroxy phosphonyl, alkyl thio, aryl thio, perfluoro alkyl thio, hydroxycarbonyl alkyl thio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,

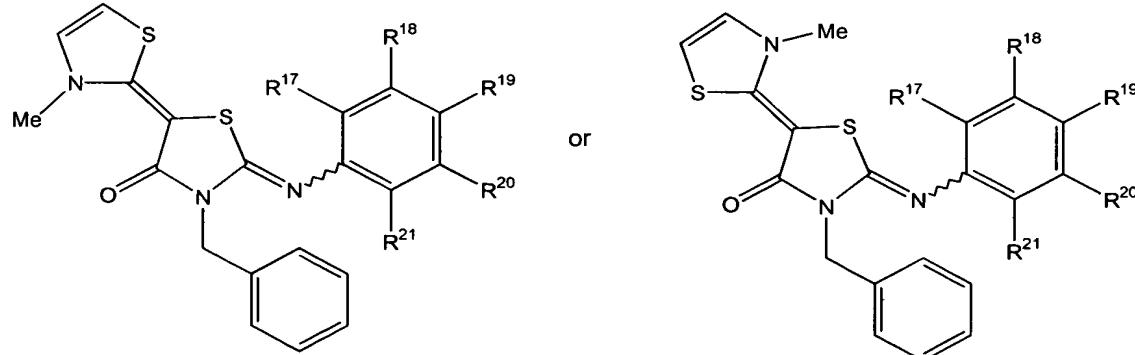
10 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkyl arylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,

15 diarylaminosulfonyl or alkyl arylaminosulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and

the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are unsubstituted or substituted with one or more substituents each independently

20 selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or alkylenedioxy.

64. The method of claim 59, wherein the compound has formulae VII:



25 or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl,

hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl,

5 alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,

10 arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,

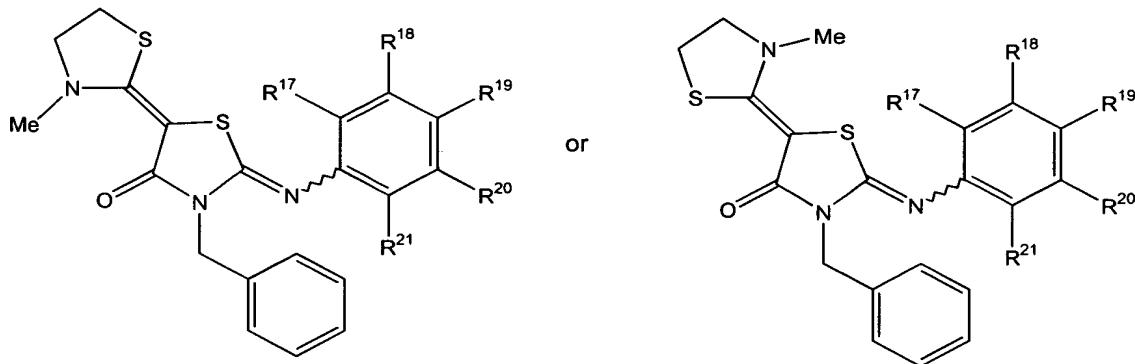
15 20 alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminalkyl,

25 30 aryloxycarbonylaminalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,

diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and

the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are unsubstituted or substituted with one or more substituents each independently selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or alkylenedioxy.

65. The method of claim 59, wherein the compound has formulae VIII:

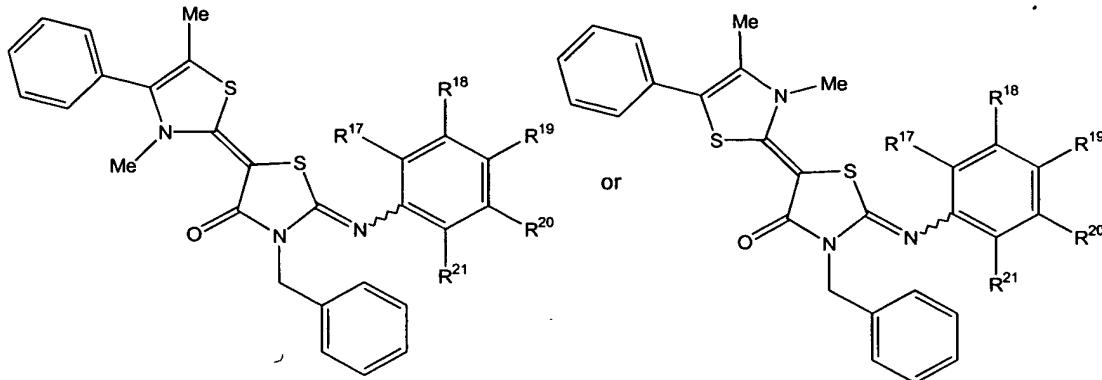


or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy,

aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,  
 alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, guanidino,  
 isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N,N'-  
 dialkylureido, N'-alkyl-N'-arylureido, N,N'-diarylureido, N'-arylureido, N,N'-  
 5 dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido,  
 N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-  
 aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido,  
 amidino, alkylamidino, arylamidino, aminothiocarbonyl,  
 alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,  
 10 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,  
 alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,  
 diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino,  
 aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,  
 aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino,  
 15 alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,  
 heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  
 $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,  
 alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio,  
 perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,  
 20 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,  
 hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy,  
 alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,  
 diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl,  
 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,  
 25 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,  
 diarylaminosulfonyl or alkylarylaminosulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$   
 and  $R^{21}$ , which substitute adjacent carbons on the ring, together form  
 alkylenedioxy; and  
 the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are  
 30 unsubstituted or substituted with one or more substituents each independently  
 selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or  
 alkylenedioxy.



66. The method of claim 59, wherein the compound has formulae IX:



or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$

5 and R<sup>21</sup> are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, 10 aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, 15 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, guanidino, 20 isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'- dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'- dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, 25 amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,

5 alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyanato, isothiocyanato,

10 alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,

15 alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylamino sulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and

the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are

20 unsubstituted or substituted with one or more substituents each independently selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or alkylenedioxy.